## REMARKS

Upon entry of this amendment, claims 79-115 will be pending. Claims 79 and 98 have been amended to recite that the non-chocolate food product is for human or veterinary animal consumption, support is found throughout the specification, no new matter was added.

**Rejection under 35 USC § 103**

The Examiner has rejected claims 79-115 as obvious over Romanczyk, Jr (US 5,554,645) in view of Wideman et al. (US 6,127,421) on the ground that Romanczyk and Wideman teach use of cocoa polyphenols and L-Arginine, respectively, for the same purpose (anti-tumor) and it would have been obvious to combine the two active ingredients into one composition for anti-tumor treatment and that adjustment of the amounts/ranges of each active ingredient is deemed merely a matter of judicious selection and routine optimization to arrive at the claimed compositions. Applicants respectfully traverse the rejection.

*Routine optimization of prior art taught away from the dosage levels of the present composition.*

At the outset, Applicants point out that Examiner acknowledges that Romanczyk does not teach the claimed amounts/ranges for anti-tumor purposes. While it does not appear that, as of the effective filing date of the present application, there were human or animal clinical trials conducted with cocoa polyphenols for treatment of cancer, for reasons discussed below, research regarding other polyphenols such as quercetin would have suggested to a person of skill in the art to administer high doses rather than optimize the amounts by reducing them as is required by the present claims.

For example, antineoplastic effects of quercetin were tested in mice at dosages of 40 mg/kg/day, which dosage was associated with a 20% increase in subject life span. However, increasing the dosage was considerably more effective—quercetin at a dosage of 80 mg/kg twice daily (*i.e.,* 160 mg/kg) was found to be more effective—at this higher dose, 94% increase in subject life span was observed (see, Attachment 1- Molnar *et al*, "Antitumor activity of flavonoids on NK/Ly ascites tumor cells." *Neoplasma*, vol. 28,

issue 1, 11-18. 1981). It is true that quercetin is a distinct compound from cocoa polyphenols recited in Applicants' claims but once cocoa polyphenols were discovered by Romanczyk to have antineoplastic properties like quercetin, one skilled in the art would have then expected that high dosages were important for the effect and would not have optimized the dose downward, *i.e.,* to arrive at the amounts recited in Applicants' claims. Assuming an average person of 70 kg, the optimum quercetin dosage of 160 mg/kg results in a dosage of 11.2 g of quercetin (5.6 g twice daily). In contrast, Applicants claims recite "up to 3 g of cocoa polyphenol."

"[A] particular parameter must first be recognized as a result-effective variable, *i.e.,* a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation." *(see,* MPEP Section 2144.05 II). Consequently, in order to make the claimed compositions obvious, the cited references (Romanczyk and Wideman) should have recognized that cocoa polyphenols of Romanczyk are effective for inducing vasodilation (rather than for anti-neoplastic effects). In other words, a person of skill in the art would have had no reason to optimize the amounts of cocoa polyphenols of Romanczyk to achieve vasodilating effects and have any reasonable expectation of success when such effects were not suggested by any of the cited references. This is because "the prior art [must] have suggested 'the kind of experimentation necessary to achieve the claimed composition" *In re Boesch*, 617 F.2d at 276 (holding that such a showing was made). *See also, In re Antonie*, 559 F.2d at 620 (holding that such a showing was not made). In *In re Antonie,* the claims at issue recited a wastewater treatment device comprising a tank having certain "treatment capacity" which capacity was a function of "tank volume." The prior art cited by the Patent Office disclosed the basic structure of Antonie's device but was silent regarding the "tank volume." The Court reversed the rejection because the cited prior art "was not trying to maximize or control 'treatment capacity';" "experiments suggested by [the cited art did] not reveal the property which applicant [had] discovered;" and "there [was] no evidence in the record that the prior art recognized that particular parameter affected the result." *Id.*

Following the reasoning in *Antonie* and *Boesch,* Romanczyk and Wideman should have suggested, to a person of skill in the art, vasodilating effects of their compounds before the experiments to optimize the amount of these compounds to achieve the vasodilating effect could have been conducted. In the absence of such a recognized result, and further because other knowledge in the art (*see* Attachment 1) suggested that polyphenol doses should be increased to optimize the anti-neoplastic effects, arriving at the amount limitations of Applicants' present claims would not have been the result of routine optimization.

This conclusion is further supported by the recent decision of the USPTO Board of Appeals and Interferences, which is also on point. In *Ex parte Buzzoni* (BPAI Appeal No. 2007-3725, U.S. Appl. Ser. No.: 10/183,478, pages 6-7 (2008)), the Appellant claimed an anchorless wheel bumper block (to be used as a stop in a parking facility), and the cited prior art disclosed a cellular arresting block (for use to slow and stop aircrafts, trucks and other vehicles). The prior art block was larger than the claimed block and the Examiner rejected the claims on the ground that it would have required routine optimization to modify the block of the prior art and arrive at the claimed block. The Board disagreed and held that the Examiner failed to establish a *prima facie* case of obviousness because he failed to establish that an optimum obtained for the cited prior art block would have also been an optimum for the Appellants' block. Here, applying *Buzzoni* to the facts of the present case, dosage optimum for anti-tumor purposes is not the same as dosage optimum for vasorelaxation purposes recited in Applicants' claims. In other words, even if one were to assume, for purposes of an argument, that it would have been obvious to optimize the amounts of compounds taught by Romanczyk and Wideman for anti-tumor purposes; the Examiner has not established (and could not have as shown above) that it would have been obvious to optimize the amounts of the compounds and arrive at those recited in the rejected claims.

In summary, the expectation that high dosages were required for anti-tumor treatment would have, at best, lead to upward optimization of Romanczyk and Wideman resulting in much higher dosages than those presently claimed and a *prima facie* case of obviousness has not been made, because not knowing vasodilating properties of cocoa

polyphenols, a person of skill in the art would not have had any reason to adjust the amounts downward to arrive at the products recited in the present claims.

*Prior art provided no reasonably expectation of success for anti-tumor treatment using L-arginine*

Applicants enclose herewith a lecture by Kenneth Park entitled "The Immunological and Metabolic Effects of L-arginine in Human Cancers" (Attachment 2, Proc. Nutrit. Soc. 52,387-401 (1993)), in which studies in animals and humans with cancer showed that L-arginine supplementation stimulated tumor growth and tumor protein synthesis, respectively. Applicants submit that, as of the effective filing date of the present application, contradictory evidence existed regarding the role of L-arginine in tumorigenesis, hence, one of skill in the art could not have predicted (from data with chicken) the anti-tumor behavior of L-arginine supplied as a human or veterinary food (as the claims now require) with a reasonable expectation of success.

Moreover, the cited Wideman reference does not even deal w/anti-tumor effects of L-arginine but only references work of another where administration of L-arginine showed that tumor-associated mortality in chicken was not significantly different between a low (0.92%) and high (2.4%) L-arginine diets. Thus, no dose-response was observed—dose-response analysis is an important criterion used for the substantiation of a cause-and-effect relationship (between compound tested and observed effect).

In view of the uncertainty in the art, a person of skill in the art would not have known if L-arginine would have had an anti-tumor effects and therefore would have had no reason to combine it with cocoa polyphenol and have any reasonable expectation of success.

* * *

Claims 109-115 are patentable for an additional reason. Claims 109-115 recite L-arginine in the amount of at least 100 mg/g (*i.e.*, 10% of the non-chocolate food product). Applicants respectfully submit that the effects of L-arginine as an anti-tumor ingredient were unpredictable and the cited references provide no motivation to create a composition with the claimed L-arginine amounts. To arrive at the presently claimed

composition, a person of skill in the art would have had to increase the L-arginine content of Wideman by more than 400% —there is no motivation to do that in the combined teachings of the cited references—a *prima facie* case of obviousness has not been made nor can it be made.

Withdraw of the rejection is respectfully requested in view of the above amendments and arguments.

**Conclusion**

In view of the above amendment and remarks, Applicants believe that the application is in condition for allowance. An action to that effect is respectfully requested.

Respectfully submitted,

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